UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/512,109	07/21/2005	Mitsuo Nishikawa	051023-0118	4547

22428 7590 11/08/2007

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
11/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/512,109	NISHIKAWA, MITSUO	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *1-5, 9-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendices A, B, C*.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 10 August 2007 has been entered in full. Claim 1 is amended. Claim 14 is cancelled.

Election/Restrictions

Applicant's election with traverse of Group II, claims 6-8 and 13-14, directed to an isolated polypeptide in the reply filed on 10 August 2007 is acknowledged. The traversal is on the ground(s) that the claims as currently amended relate to a single inventive concept and should be examined together. Applicant argues that the present claims are not subject to the stated grounds for the alleged lack of unity, namely, that Warren et al. (W0/0260942) is anticipatory of claim 1 by virtue of teaching "an isolated DNA sequence that encodes a polypeptide that is 99.5% identical to SEQ ID N0:48." This is not found persuasive because the instant claims are directed to a polypeptide comprising the amino acid sequence of SEQ ID NO: 48 as well as an amino acid sequence including deletion, substitution, or insertion of one or several amino acids in the amino acid sequence of SEQ ID NO: 48. Warren et al. (with priority to 1/31/01) teach a polypeptide that is 99.5% identical to the amino acid sequence of SEQ ID NO: 48 of the instant application (see SEQ ID NO: 12 of Warrant et al.; please see sequence alignment attached to the instant Office Action as Appendix C). Thus, claims 6-8 and 13 lack a special technical feature and cannot share one with the other claims.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-5, 9-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in the reply filed on 10 August 2007.

Claims 6-8 and 13 are under consideration in the instant application.

Specification

1. The disclosure is objected to because of the following informalities:

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see for example, page 23, line 26). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "POLYPEPTIDE HAVING AN ACTIVITY TO SUPPORT PROLIFERATION OR SURVIVAL OF HEMATOPOIETIC STEM OR PROGENITOR CELLS".

Appropriate correction is required.

Claim Objections

4. Claim 6 is objected to because of the following informalities:

4a. Claim 6 depends from claims 1 and 2, which are currently withdrawn.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 6-8 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Claims read on a product of nature in that the claimed polypeptide is not "isolated". In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty,* 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified" as taught by pages 74-76 of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 6-8 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 48 and a composition thereof, *does not reasonably provide enablement for* an amino acid sequence including deletion, substitution or insertion of one or several amino acids in the amino acid sequence of SEQ ID NO: 48 and a pharmaceutical composition comprising such. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 6-8 are directed to a polypeptide encoded by the DNA molecule of SEQ ID NO: 47 or a nucleic acid that hybridizes thereto, the polypeptide having an activity to support proliferation or survival of hematopoietic stem cells or hematopoietic progenitor cells. The

claims recite that the polypeptide comprises the amino acid sequence of SEQ ID NO: 48, or an amino acid sequence including deletion, substitution or insertion of one or several amino acids in the amino acid sequence of SEQ ID NO: 48. Claim 8 recites that the polypeptide may be modified with one or more agents. Claim 13 is directed to a pharmaceutical composition comprising the polypeptide.

The specification of the instant application teaches that AGM-s3-A9 stromal cells in which murine SCR-6 (SEQ ID NO: 23) was highly expressed were prepared (page 75, lines 7-10). The specification also discloses that human hematopoietic stem/progenitor cells and stromal cells expressing SCR-6 were co-cultured and the determination of proliferation statuses of hematopoietic stem cells and hematopoietic progenitor cells was made by clonogenic assay (page 75, lines 11-22). The specification at pages 75-76 teaches that the co-culture with AGM-s3-A9 cells in which SCR-6 was highly expressed increases BFU-E and CFU-C and refers to Figure 9. The specification concludes that the activity to support hematopoietic stem cells or hematopoietic progenitor cells, of AGM-s3-A9 increases by allowing SCR-6 to be highly expressed, and thus, the gene product of SCR-6 has an activity to support the survival or proliferation of hematopoietic stem or progenitor cells (page 76, lines 7-13). However, after reviewing Figure 9, it appears to the Examiner that the data do not support the claims. For example, the claimed SCR-6 protein expressed by stromal cells (A9/SCR-6) seems to stimulate proliferation of erythroid progenitors (BFU-E) and all colony forming unit progenitor culture cells (CFU-C) as compared to stromal cells alone (A9). Yet, the stromal cells containing vector control (A9/pMXIG) have a much greater increase in total CFU-C than both the stromal cells expressing SCR-6 and control cells. It is not clear as to why the total CFU-C for the vector

control far outnumber the CFU-C for SCR-6. In other words, why does the introduction of the pMXIG control vector in the stromal cells give the CD34+ cells a selective growth advantage? Does the claimed SCR-6 polypeptide only stimulate the proliferation of erythroid progenitor cells? Applicant is encouraged to clarify the data presented in Figure 9.

Additionally, there are no methods or working examples in the specification to indicate that the SCR-6 protein of SEQ ID NO: 23 or 48 supports the proliferation of hematopoietic *stem* cells. The experiments disclosed in the instant specification only monitor erythroid burst-forming unit (BFU-E) colonies and colony forming unit progenitor culture cells (CFU-C). It is well known in the art that colony-forming cells (CFCs) are considered to comprise a large, intermediate progenitor compartment that spans the entire stepwise process of lineage restriction (Wognum et al., Arch Med Res 34: 461-475, 2003), while BFU colonies are primitive erythroid progenitors (Quesenberry et al., "Hematopoietic stem cells, progenitor cells, and cytokines", pages 153-174, Williams Hematology, Sixth Edition, New York: McGraw-Hill, 2001; especially page 155, Table 14-1). Finally, there are no methods or working examples in the specification to indicate that the SCR-6 protein of SEQ ID NO: 23 or 48 supports the *survival* of hematopoietic stem or progenitor cells. The experiments in the instant application have only examined the proliferative response of progenitor cells upon the co-culturing of CD34+ hematopoietic stem/progenitor cells with stromal cells (page 76, lines 1-3). A large quantity of experimentation would be required of the skilled artisan to determine if the claimed SCR-6 polypeptide supports or enhances the survival of hematopoietic stem or progenitor cells. Such experimentation is considered undue. There is also little guidance provided in the instant specification for one skilled in the art to determine such.

Relevant literature teaches that growth factors oftentimes have diverse and overlapping functions. For example, IL-10 inhibits cytokine production, modulates immune cells and stimulates mast cells (Quesenberry et al., page 157, Table 14-3) while kit ligand (SCF) stimulates the survival and growth of primitive stem cells and enhances the generation of mast cells (Quesenberry et al., page 157, Table 14-4). Quesenberry et al. even state that "[m]ost cytokines have many actions on different lineages and stages of differentiation" (page 156, column 2, 1st full paragraph). Several growth factors may not act on early progenitors alone, but rather, act in combination with other cytokines (see for instance, EPO, IL-1, IL-4, IL-9, Flt-3 ligand (Quesenberry et al., page 157, Tables 14-3 and 14-4). Additionally, a number of growth factors may exhibit inhibitory effects on early, more primitive stem cells, while stimulating the more differentiated progeny (Quesenberry et al., page 158, Table 14-5; bottom of page 161 through the top of page 162). Thus, based upon the state of the art at the time the application was filed and the data presented in Figure 9, one skilled in the art would not be able to predict the activity of the claimed SCR-6 polypeptide of SEQ ID NO: 48. A large quantity of experimentation would be required of the skilled artisan to determine such.

(ii) It is noted that claims 6-8 and 13 encompass an amino acid sequence including deletion, substitution or insertion of one or several amino acids in the amino acid sequence of SEQ ID NO: 48. Thus, the claims encompass an infinite number of variants, fragments, and derivatives of the amino acid sequence of SEQ ID NO: 48. The specification of the instant application teaches that the polypeptides of the present invention also comprise polypeptides having amino acid sequences in which one or several amino acids are substituted, deleted or inserted in the

amino acid sequence represented in SEQ ID NO: 48 and having activity to support hematopoietic stem cells (page 22, lines 1-9). The specification also discloses that for the amino acid deletion, the polypeptide may be a fragment which lacks an amino acid sequence at the N-terminal end and/or the C-terminal end (page 23, lines 3-5). However, the specification does not teach any variant, fragment, or derivative of the SCR-6 polypeptide other than the full-length amino acid sequence of SEQ ID NO: 48. The specification also does not teach functional or structural characteristics of the polypeptide variants, fragments, and derivatives recited in the claims.

The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the DNA and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Even if an

active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Relevant literature reports examples of polypeptide mutations which alter the normal activity of the polypeptide. For example, Wuyts et al. (J Immunol 163: 6155-6163, 1999) establish that NH_2-and COOH- terminal truncations of granulocyte chemotactic protein-2 (GCP-2) have enhanced neutrophil chemotactic potency as compared to wild-type GCP-2 (abstract; pg 6157-6158). Sher et al. (J Biol Chem 274(49):35016-35022, 1999) disclose that keratinocyte growth factor (FGF-7) acts predominantly on cells of epithelial origin and regulates processes in embryonal and adult development, including cell growth, differentiation, cell migration, and repair of epithelial tissues (pg 35016, ¶ 1). Sher et al. demonstrate that point mutations in a loop of FGF-7 do not alter receptor binding affinity, but cause reduced mitogenic potency and reduced ability to induce receptor-mediated phosphorylation events (pg 35020-35021). Additionally, a SCF mutant called $Steel^{17H}$ (Sl^{17H}) induces melanocyte defects and sterility in males. The Sl^{17H} allele contains a mutation that results in the substitution of 36 amino acids in the SCF cytoplasmic domain with 28 novel amino acids (Kapur et al., Blood 94(6): 1915-1925,

1999). Kapur et al. teach that compound heterozygous Sl/Sl^{17H} mice manifest several hematopoietic abnormalities in vivo, such as red blood cell deficiency, bone marrow hyperplasia, and defective thymopoiesis (pg 1917-1918; Figures 2-3). In vitro, both the soluble and membrane-associated Sl^{17H} isoforms exhibit reduced cell surface expression on stromal cells and diminished biological activity as compared to wild soluble and membrane-associated forms (abstract, pg 1919-1921; Figures 6-7). Finally, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48). Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, the specification fails to teach the skilled artisan how to make and use biologically active SCR-6 variants without resorting to undue experimentation to determine what the specific biological activities of the variants are.

(iii) Furthermore, it is noted that claim 13 is directed to a pharmaceutical composition comprising (i) a polypeptide comprising the amino acid sequence of SEQ ID NO: 48 or (ii) an amino acid sequence including deletion, substitution, or insertion of one or several amino acids in the amino acid sequence of SEQ ID NO: 48. The specification teaches a composition comprising an isolated SCR-6 polypeptide consisting of the amino acid sequences of SEQ ID NO: 48. The specification does not teach how to use an SCR-6 "pharmaceutical" composition without undue experimentation for the treatment of a disease or disorder in an animal. The specification lists disorders to be treated (pg 40, lines 11-19), but there are no working examples directed to a particular disorder in an animal or administration of the SCR-6 polypeptide

comprising the amino acid sequence of SEQ ID NO: 48 to an animal for treatment. There is also little guidance in the specification or working examples that indicate the SCR-6 polypeptide of SEQ ID NO: 48 supports the proliferation or survival of hematopoietic stem cells or progenitor cells *in vivo*. Undue experimentation would also be required of the skilled artisan to determine the optimal dosage, duration, and route of administration of the SCR-6 polypeptide if administered *in vivo*. (Note, this issue could be overcome by deleting the word "pharmaceutical" from the claims.)

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and screen same for activity, as well as to determine the quantity of the polypeptide to be administered, the most effective administration route, and the duration of the treatment; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

7. Claims 6-8 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 6-8 are directed to a polypeptide encoded by the DNA molecule of SEQ ID NO: 47 or a nucleic acid that hybridizes thereto, the polypeptide having an activity to support proliferation or survival of hematopoietic stem cells or hematopoietic progenitor cells. The claims recite that the polypeptide comprises the amino acid sequence of SEQ ID NO: 48, or an amino acid sequence including deletion, substitution or insertion of one or several amino acids in the amino acid sequence of SEQ ID NO: 48. Claim 8 recites that the polypeptide may be modified with one or more agents. Claim 13 is directed to a pharmaceutical composition comprising the polypeptide. The claims do not require that the polypeptide possess any particular conserved structure. Thus, the claims are drawn to a genus of polypeptides.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a functional requirement that the polypeptide has an activity to support hematopoietic stem cell or hematopoietic progenitor cell proliferation or survival. There is not even identification of any particular portion of the structure of the polypeptide that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of one polynucleotide species (SEQ ID NO: 47) and one polypeptide species (SEQ ID NO: 48) is not adequate written description of an entire genus of functionally equivalent

polynucleotides and polypeptides which incorporate all variants and fragments of the DNA sequence of SEQ ID NO: 47 and the polypeptide sequence of SEQ ID NO: 48.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated polypeptide consisting of the amino acid sequence of SEQ ID NO: 48 or an isolated polypeptide encoded by the nucleic acid sequence of SEQ ID NO: 47, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first

paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 6-8 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Ceccardi et al. (US 2003/0022217; priority to 02 July 2001).

Ceccardi et al. teach an isolated polypeptide that is 100% identical to the polypeptide of SEQ ID NO: 48 of the instant application (see SEQ ID NO: 2 of Ceccardi et al.; see sequence alignment attached to the instant Office Action as Appendix A). Ceccardi et al. disclose an isolated polynucleotide that encodes the polypeptide of SEQ ID NO : 48 of the instant application (see SEQ ID NO: 1 of Ceccardi et al.; see also sequence alignment attached to the instant Office Action as Appendix B). Ceccardi et al. also teach that modifications may be made to the polypeptide, such as the addition of polyethylene glycol (page 6, [0054]). Ceccardi et al. teach a polypeptide composition utilized in several different in vitro assays (page 6, [0056]).

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
18 October 2007

Bridget E. Bunner

BRIDGET E. BUNNER
PRIMARY EXAMINER

Appendix A

```
<!--StartFragment-->RESULT 1
US-10-185-770-2
; Sequence 2, Application US/10185770
; Publication No. US20030022217A1
; GENERAL INFORMATION:
;  APPLICANT: CECCARDI, Toni et al.
;  TITLE OF INVENTION: ISOLATED HUMAN SECRETED PROTEINS,
;  TITLE OF INVENTION:  NUCLEIC ACID MOLECULES ENCODING HUMAN SECRETED PROTEINS, AND
;  TITLE OF INVENTION:  USES THEREOF
;  FILE REFERENCE: CL0001247
;  CURRENT APPLICATION NUMBER: US/10/185,770
;  CURRENT FILING DATE:  2002-07-01
;  PRIOR APPLICATION NUMBER: 60/301,852
;  PRIOR FILING DATE: 2001-07-02
;  NUMBER OF SEQ ID NOS: 4
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 2
;   LENGTH: 243
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-185-770-2

  Query Match             100.0%;  Score 1381;  DB 4;  Length 243;
  Best Local Similarity   100.0%;  Pred. No. 2.3e-114;
  Matches  243;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MQFRLFSFALIILNCMDYSHCQGNRWRRSKRASYVSNPICKGCLSCSKDNGCSRCQQKLF 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQFRLFSFALIILNCMDYSHCQGNRWRRSKRASYVSNPICKGCLSCSKDNGCSRCQQKLF 60

Qy         61 FFLRREGMRQYGECLHSCPSGYYGHRAPDMNRCARCRIENCDSCFSKDFCTKCKVGFYLH 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 FFLRREGMRQYGECLHSCPSGYYGHRAPDMNRCARCRIENCDSCFSKDFCTKCKVGFYLH 120

Qy        121 RGRCFDECPDGFAPLEETMECVEGCEVGHWSEWGTCSRNNRTCGFKWGLETRTRQIVKKP 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 RGRCFDECPDGFAPLEETMECVEGCEVGHWSEWGTCSRNNRTCGFKWGLETRTRQIVKKP 180

Qy        181 VKDTILCPTIAESRRCKMTMRHCPGGKRTPKAKEKRNKKKKRKLIERAQEQHSVFLATDR 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VKDTILCPTIAESRRCKMTMRHCPGGKRTPKAKEKRNKKKKRKLIERAQEQHSVFLATDR 240

Qy        241 ANQ 243
              |||
Db        241 ANQ 243
<!--EndFragment-->
```

Appendix B

<!--StartFragment-->RESULT 1
US-10-185-770-1
; Sequence 1, Application US/10185770
; Publication No. US20030022217A1
; GENERAL INFORMATION:
; APPLICANT: CECCARDI, Toni et al.
; TITLE OF INVENTION: ISOLATED HUMAN SECRETED PROTEINS,
; TITLE OF INVENTION: NUCLEIC ACID MOLECULES ENCODING HUMAN SECRETED PROTEINS, AND
; TITLE OF INVENTION: USES THEREOF
; FILE REFERENCE: CL0001247
; CURRENT APPLICATION NUMBER: US/10/185,770
; CURRENT FILING DATE: 2002-07-01
; PRIOR APPLICATION NUMBER: 60/301,852
; PRIOR FILING DATE: 2001-07-02
; NUMBER OF SEQ ID NOS: 4
; SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 1
; LENGTH: 732
; TYPE: DNA
; ORGANISM: Homo sapiens
US-10-185-770-1

Alignment Scores:

Pred. No.:	4.88e-152	Length:	732
Score:	1381.00	Matches:	243
Percent Similarity:	100.0%	Conservative:	0
Best Local Similarity:	100.0%	Mismatches:	0
Query Match:	100.0%	Indels:	0
DB:	6	Gaps:	0

US-10-512-109-48 (1-243) x US-10-185-770-1 (1-732)

```
Qy          1 MetGlnPheArgLeuPheSerPheAlaLeuIleIleLeuAsnCysMetAspTyrSerHis 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ATGCAGTTTCGCCTTTTCTCCTTTGCCCTCATCATTCTGAACTGCATGGATTACAGCCAC 60

Qy         21 CysGlnGlyAsnArgTrpArgArgSerLysArgAlaSerTyrValSerAsnProIleCys 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TGCCAAGGCAACCGATGGAGACGCAGTAAGCGAGCTAGTTATGTATCAAATCCCATTTGC 120

Qy         41 LysGlyCysLeuSerCysSerLysAspAsnGlyCysSerArgCysGlnGlnLysLeuPhe 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 AAGGGTTGTTTGTCTTGTTCAAAGGACAATGGGTGTAGCCGATGTCAACAGAAGTTGTTC 180

Qy         61 PhePheLeuArgArgGluGlyMetArgGlnTyrGlyGluCysLeuHisSerCysProSer 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TTCTTCCTTCGAAGAGAAGGGATGCGCCAGTATGGAGAGTGCCTGCATTCCTGCCCATCC 240

Qy         81 GlyTyrTyrGlyHisArgAlaProAspMetAsnArgCysAlaArgCysArgIleGluAsn 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 GGGTACTATGGACACCGAGCCCCAGATATGAACAGATGTGCAAGATGCAGAATAGAAAAC 300

Qy        101 CysAspSerCysPheSerLysAspPheCysThrLysCysLysValGlyPheTyrLeuHis 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 TGTGATTCTTGCTTTAGCAAAGACTTTTGTACCAAGTGCAAAGTAGGCTTTTATTTGCAT 360

Qy        121 ArgGlyArgCysPheAspGluCysProAspGlyPheAlaProLeuGluGluThrMetGlu 140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 AGAGGCCGTTGCTTTGATGAATGTCCAGATGGTTTTGCACCATTAGAAGAAACCATGGAA 420

Qy        141 CysValGluGlyCysGluValGlyHisTrpSerGluTrpGlyThrCysSerArgAsnAsn 160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 TGTGTGGAAGGATGTGAAGTTGGTCATTGGAGCGAATGGGGAACTTGTAGCAGAAATAAT 480

Qy        161 ArgThrCysGlyPheLysTrpGlyLeuGluThrArgThrArgGlnIleValLysLysPro 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 CGCACATGTGGATTTAAATGGGGTCTGGAAACCAGAACACGGCAAATTGTTAAAAAGCCA 540

Qy        181 ValLysAspThrIleLeuCysProThrIleAlaGluSerArgArgCysLysMetThrMet 200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 GTGAAAGACACAATACTGTGTCCAACCATTGCTGAATCCAGGAGATGCAAGATGACAATG 600

Qy        201 ArgHisCysProGlyGlyLysArgThrProLysAlaLysGluLysArgAsnLysLysLys 220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 AGGCATTGTCCAGGAGGGAAGAGAACACCAAAGGCGAAGGAGAAGAGGAACAAGAAAAAG 660
```

Appendix B(cont.)

```
Qy        221 LysArgLysLeuIleGluArgAlaGlnGluGlnHisSerValPheLeuAlaThrAspArg 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 AAAAGGAAGCTGATAGAAAGGGCCCAGGAGCAACACAGCGTCTTCCTAGCTACAGACAGA 720

Qy        241 AlaAsnGln 243
              |||||||||
Db        721 GCTAACCAA 729
<!--EndFragment-->
```

Appendix C

<!--StartFragment-->ABG76508
ID ABG76508 standard; protein; 243 AA.
XX
AC ABG76508;
XX
DT 05-NOV-2002 (first entry)
XX
DE DNA encoding protein modification and maintenance molecule #12.
XX
KW Protein modification and maintenance molecule; gastrointestinal disorder;
KW dysphagia; esophageal spasm; gastritis; anorexia; nausea; hypertension;
KW cardiovascular disorder; atherosclerosis; vasculitis; aneurysm; allergy;
KW ischaemic heart disease; autoimmune disorder; inflammatory disorder;
KW acquired immunodeficiency syndrome; AIDS; ankylosing spondylitis; cancer;
KW anaemia; amyloidosis; cell proliferative; arteriosclerotic bursitis;
KW cirrhosis; developmental disorder; renal tubular acidosis; anaemia;
KW bone resorption; epilepsy; epithelial disorder; keratosis pilaris;
KW allergic contact dermatitis; insect bite; keloid; dermatofibroma; eczema;
KW neurological disorder; stroke; cerebral neoplasm; Alzheimer's disease;
KW Huntington's disease; dementia; reproductive disorder; infertility;
KW endometriosis; gynecomastia; ectopic pregnancy; gene therapy.
XX
OS Homo sapiens.
XX
PN WO200260942-A2.
XX
PD 08-AUG-2002.
XX
PF 30-JAN-2002; 2002WO-US002813.
XX
PR 31-JAN-2001; 2001US-0265705P.
PR 05-FEB-2001; 2001US-0266762P.
PR 16-FEB-2001; 2001US-0269581P.
PR 23-FEB-2001; 2001US-0271198P.
PR 01-MAR-2001; 2001US-0272813P.
PR 13-MAR-2001; 2001US-0275586P.
PR 23-MAR-2001; 2001US-0278505P.
PR 30-MAR-2001; 2001US-0280539P.
XX
PA (INCY-) INCYTE GENOMICS INC.
XX
PI Warren BA, Honchell CD, Lu Y, Walia NK, Burford N, Delegeane AM;
PI Gandhi AR, Baughn MR, Griffin JA, Gietzen KJ, Lu DAM, Ison CH;
PI Ramkumar J, Tang TY, Lal PG, Borowski ML, Duggan BM, Hafalia AJA;
PI Arvizu C, Thangavelu K, Yao MG, Elliott VS, Ding L, Yue H, Lee S;
PI Swarnakar A, Tran UK, Xu Y;
XX
DR WPI; 2002-608499/65.
DR N-PSDB; ABS58379.
XX
PT New protein modification and maintenance molecules useful for treating or
PT preventing gastrointestinal, cardiovascular, autoimmune/inflammatory,
PT cell proliferative, developmental, neurological and reproductive
PT disorders.
XX
PS Claim 1; Page 151; 172pp; English.
XX
CC The invention describes an isolated human polypeptide (I), a naturally
CC occurring amino acid sequence at least 90 % identical to the protein, or
CC a biologically active fragment or an immunogenic fragment of the protein.
CC The protein modification and maintenance molecules are useful in the
CC diagnosis, treatment, and prevention of gastrointestinal (e.g. dysphagia,
CC esophageal spasm, gastritis, anorexia or nausea), cardiovascular (e.g.
CC atherosclerosis, hypertension, vasculitis, aneurysms, or ischaemic heart
CC disease), autoimmune/inflammatory (e.g. acquired immunodeficiency
CC syndrome (AIDS), allergies, ankylosing spondylitis, anaemia or
CC amyloidosis), cell proliferative (e.g. cancers, arteriosclerotic,
CC bursitis, or cirrhosis), developmental (e.g. renal tubular acidosis,
CC anaemia, bone resorption, or epilepsy), epithelial (e.g. allergic contact
CC dermatitis, keratosis pilaris, insect bites, keloid, dermatofibroma or
CC eczema), neurological (e.g. stroke, cerebral neoplasms, Alzheimer's
CC disease, Huntington's disease or dementia), and reproductive disorders
CC (e.g. infertility, endometriosis, gynecomastia or ectopic pregnancy).
CC These may also be used in assessing the effects of exogenous compounds on
CC the expression of nucleic acid and amino acid sequences of protein
CC modification and maintenance molecules. Polynucleotides are useful in

Appendix C

```
CC   somatic and germline gene therapy. This is the amino acid sequence of a
CC   protein modification and maintenance molecule described in the invention
XX
SQ   Sequence 243 AA;

  Query Match             99.5%;  Score 1374;  DB 5;  Length 243;
  Best Local Similarity   99.6%;  Pred. No. 4.7e-104;
  Matches  242;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQFRLFSFALIILNCMDYSHCQGNRWRRSKRASYVSNPICKGCLSCSKDNGCSRCQQKLF 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQFRLFSFALIILNCMDYSHCQGNRWRRSKRASYVSNPICKGCLSCSKDNGCSRCQQKLF 60

Qy         61 FFLRREGMRQYGECLHSCPSGYYGHRAPDMNRCARCRIENCDSCFSKDFCTKCKVGFYLH 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 FFLRREGMRQYGECLHSCPSGYYGHRAPDMNRCARCRIENCDSCFSKDFCTKCKVGFYLH 120

Qy        121 RGRCFDECPDGFAPLEETMECVEGCEVGHWSEWGTCSRNNRTCGFKWGLETRTRQIVKKP 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 RGRCFDECPDGFAPLEETMECVEGCEVGHWSEWGTCSRNNRTCGFKWGLETRTRQIVKKP 180

Qy        181 VKDTILCPTIAESRRCKMTMRHCPGGKRTPKAKEKRNKKKKRKLIERAQEQHSVFLATDR 240
              ||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VKDTIPCPTIAESRRCKMTMRHCPGGKRTPKAKEKRNKKKKRKLIERAQEQHSVFLATDR 240

Qy        241 ANQ 243
              |||
Db        241 ANQ 243
<!--EndFragment-->
```